I Am Eating for Two: Parental Effects of Diet on the Offspring

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Obesity in Pregnancy

Prevalence of obesity in women aged 18 years and over (BMI ≥30 kg/m²) in 2014
Percentage of Children Who Are Obese in 2009

Predicting Preschooler Obesity at Birth: The Role of Maternal Obesity in Early Pregnancy
Robert C. Whitaker, MD, MPH
Pediatrics, 2004

TABLE 5. Logistic Regression Models Showing Adjusted Odds* of Obesity (BMI > 5th Percentile) at Various Preschool Ages

Developmental Origins of Adult Disease: “Barker Hypothesis”

- Developmental Plasticity: a single genotype, when influenced by specific intrauterine events, can create multiple phenotypes
- There are specific windows of plasticity during which a developing organism is sensitive to the environmental surroundings
What are the windows of exposure leading to long-term outcomes?

- Oocyte
- In utero
- Childhood

Association between pre-pregnancy overweight or obesity and large for gestational age offspring

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Pre-pregnancy Overweight or Obesity</th>
<th>Large for Gestational Age Offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yu et al., PLoS One 2013</td>
<td>500</td>
<td>30%</td>
<td>10%</td>
</tr>
<tr>
<td>Järvenel et al. 2012</td>
<td>1000</td>
<td>40%</td>
<td>10%</td>
</tr>
<tr>
<td>Lai et al. 2013</td>
<td>500</td>
<td>20%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Obesity impairs oocyte development

- Smaller size
- Increased degeneration
- Decreased fertilization rates

Jungheim et al. Endocrinology, 2010
Sasson et al. Diabetologia, 2014
Maternal Obesity Impairs Mitochondrial Function in Oocytes

- The oocyte depends on its mitochondria for ATP production and maintenance of cellular homeostasis
- Mitochondrial DNA copy number increases over 30-fold during the stages of oocyte maturation
- The mitochondrial content of the oocyte must be sufficient to allow adequate numbers to be distributed to each cell of the embryo

Lean Obese

Does a “bad egg” make a “bad” embryo?

From Abnormal Mitochondria to Abnormal Offspring

Wu et al, Development, 2015
O’Neill et al, 2015
Maternal Obesity Alters Embryo Metabolism

Leary et al, Human Develop, 2015

What can animal studies tell us?

Experimental Design: Reciprocal Embryo Transfers

Ike Sasson MD, PhD
Exposure to pre-gestational or gestational maternal obesity results in fetal growth restriction throughout gestation

Postnatal Fate of the Offspring

Offspring from obese dams develop obesity in adulthood
Glucose tolerance is impaired in adult male offspring, but normal in female offspring with a pre or a gestational exposure to maternal obesity.

**Mechanisms of programming of the oocyte**

![Flowchart](chart.png)

Rando, Simmons Cell, 2016
So, what about the dad?

**Fat Dad, Fat Kid**

Han et al, BMJ, 2015

Contributions of maternal and paternal adiposity and smoking to adult offspring adiposity and cardiovascular risk: the Midspan Family Study

What Can Animal Studies Tell Us?
Paternal obesity impairs metabolic function in female offspring in adulthood

Ng et al, 2010

Mechanisms

- Epigenetics
- Paternal transfer of microbiota to mates
- Effects of seminal fluid on maternal behavior or physiology

Epigenetics

- the study of changes in gene function that are mitotically and/or meiotically heritable and that do not involve a change in the sequence of DNA
Agouti mice have identical genotypes but very different phenotypes due to epigenetic marks.
Obesity induced epigenetic modifications in the gametes result in programming of adult disease in the offspring.
Summary

• Pre-pregnancy overweight and obesity cause obesity in the offspring
• Both maternal and paternal obesity program offspring
• Outcomes are worse in males of obese moms
• Outcomes are worse in females of obese dads
• Mechanisms
  – impaired mitochondria function in oocytes
  – Epigenetic modifications in germ cells

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